

November 3, 1955

Dear Aaron:

When we got back to Madison, I thought a little more about the problem we discussed at Detroit, carryover effects in Lac-, and realized that we had actually studied the matter in some detail. Actually, the best test of carryover would be among Lac- segregants from Lac+/Lac₁- diploids, and we never have detected the sort of unstable Lac+ condition you mention. Whenever a lactose-positive was unstable, this was associated with instability for the other markers, and can be ascribed therefore to heterozygosity. I am quite sure I had done just the experiment you would ask for, namely to test Lac+ segregants that appear on EMB lactose agar and test their stability after passage on a non-lactose medium with definitely negative results. In addition, there is the evident linkage of V₆-Lac₁ among segregants that were obtained and maintained on EMB lactose agar (table 7, CSH 1951, p.422). Altogether, among ~~LXXXXXX~~ 125 Lac+, only 8 carried the V₆ marker assigned to the Lac- strand; if these were spurious Lac+ I am certain this would have been detected. The numbers can be put the other way, of 126 segregants that carried the V₆ marker assigned to the Lac- strand, only 8 were Lac+ (and are plausibly crossovers). Finally, in diploids which are Lac₄-Lac₁+/Lac₄+Lac₁-, the diploid is a (variegated) lactose positive on EMB lactose agar; there are many Lac₁- segregants; pure lactose-positives are practically nonexistent, as might be expected from carryover.

From these experiments, I would think that the "phenotypically masked" Lac₁- cannot be stable lactose-positives on EMB lactose; nor can they be unstable positives, or they would have been picked up by discrepancies between segregation of Lac and other markers.

In conclusion, I am willing to bet you will not find the effect you are looking for on EMB agar. However, I do think that the segregations from Lac+/Lac₁- diploids are the best material in which to look for the masking (I did at least mention this in my paper on the aberrant diploids). It might be quite rare, and perhaps not implausible it ~~might~~ might not show up very well on EMB agar: for example, you might have to keep the cells ~~going~~ growing on a more favorable medium, and perhaps use a more delicate test for masking than a positive reaction on EMB, perhaps growth rate on low concentrations of lactose. If you are still interested, I will see if we have or can make another proper diploid of the constitution Lac₁-V₆^r / Lac+ V₆^s; you could then pick segregants as being V₆^r and look among them for your effect. I forgot to say that happily for these purposes, the diploids were almost invariably kept and studied on lactose media. I am inclined to think that if there is an effect, it will be second order in regard to phenotype or frequency; I think we have already ruled out a masking that would be comparable to Sol's quondam claims on melibiase in yeast. The use of the diploids would be tricky enough that I suggest we talk it over in detail when you visit. I will also have a Lac₁- V₆^s and a Lac+ V₆^r ready for you to ~~use~~ use in the transduction experiment, which deserves to be tried on a purely empirical basis— you will have to get Pl(K-12) from Lennox. Monod also has had a rather inadequate blurb on this general subject (Bioch. Soc. Symp. 4:(1950)), and that cross was Lac-F+ x Lac-F-, as were some of my own of the same design that I don't know whether I bothered to record anywhere or not. Best to JADA; do let us know you are visiting soon.

Sincerely,

